

### REMARKS

This paper is in response to the Office Action mailed on October 13, 2004.

Claims 1, 25, 44 and 45 are amended, no claims are canceled, and claim 46 and 47 are added; as a result, claims 1-19 and 25-47 are now pending in this application.

Claim 1 is amended to clarify the claim. The amendment is not narrowing and not made in response to any valid, substantive rejection.

Claim 25 is amended to clarify the claim. The amendment is not narrowing and not made in response to any valid, substantive rejection.

Claim 44 is amended to clarify the claim.

Claim 45 is amended. This amendment is broadening.

### §112 Rejection of the Claims

Claims 33 and 40 were rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The office action states that the claim(s) contain subject matter which was not described in the specification in such a way as to reasonably enable one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully traverses.

With respect to claim 33, applicant points the examiner to page 14, lines 1-2 where applicant discloses "the temperature sensors 16 can, for example, be realized as resistance temperature sensors of a nickel chromium thick film." Applicant still further points to claim 5 as originally filed. These are two examples of where the present specification reasonably conveys to one of skill in the relevant art that the inventor had possession of the invention at the time the application was filed.

With respect to claim 40, applicant points the examiner to specification page 7, lines 7-9; 18-20; and 21-22. Applicant further points the examiner to page 9, lines 25-27. Applicant further points to page 10, lines 1-5. Applicant still further points to specification page 18, lines 8-10. Applicant further points to claim 20 as originally filed, which stated "... for an almost simultaneous performance of reprocessing reactions and/or conditioning reactions and a chip-based characterization of the products." These are obvious examples of where the present

specification reasonably conveys to one of skill in the relevant art that the inventor had possession of the invention at the time the application was filed.

Claims 25-30 and 44-45 were rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses. Claims 25, 44 and 45 as they previously stood were particularly pointed out and distinctly claimed. Applicant requests reconsideration and withdrawal of these rejections.

#### §102 Rejection of the Claims

Claims 1-5, 8-10, 12-15, 17-19, 25-36 and 38-45 were rejected under 35 USC § 102(b) as being anticipated by Lipshutz et al. (U.S. Patent No. 5,856,174). Applicant respectfully traverses as a *prima facie* case of anticipation has not been established.. It is of course fundamental that in order to sustain an anticipation rejection that each and every step or element in the rejected claim must be taught or suggested in the cited reference. To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. V. Guardian Industries Corp.*, 75 F.3d 1558, 37 USPQ2d 1618 (Fed. Cir. 1996). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Here, Lipshutz fails to teach “a single reaction chamber” as recited in independent claim 1 or a “a single chamber” as recited in independent claim 25.

Independent claim 1 recites, in part, “the capillary gap forms a single reaction chamber that is adapted to amplify and characterize nucleic acids therein.” Applicant can not find these features in Lipshutz. In fact Lipshutz teaches that the amplification and characterization occur in distinct chambers.

The Office Action at page 12 states that

the device of Lipshutz comprises a chamber comprising a chamber body and optically permeable support sealed together to form a capillary gap (ie well or cavity space forming the reaction chamber between the body and support, Column 15, lines 14-17) whereby the gap forms a single reaction chamber.

Lipshutz at Column 15, lines 9-20 states

As an example, the wells manufactured into the surface of one planar member make up the various reaction chambers of the device. Channels manufactured into the surface of this or another planar member make up fluid channels which are used to fluidly connect the various reaction chambers. Another planar member is then placed over and bonded to the first, whereby the wells in the first planar member define cavities within the body of the device which cavities are the various reaction chambers of the device. Similarly, fluid channels manufactured in the surface of one planar member, when covered with a second planar member define fluid passages through the body of the device (emphasis added).

Accordingly, Lipshutz requires various, that is, a plurality of reaction chambers. The question now is does Lipshutz teach that any single one of its various reaction chambers is adapted to amplify and characterize nucleic acids therein. Applicant submits that Lipshutz does not teach this feature of claim 1.

Lipshutz at col. 2, lines 23-27 states “a fluid transport system for moving a fluid sample from at least a *first reaction chamber* of said plurality of reaction chambers to at least a *second reaction chamber* of said plurality of reaction chambers and a *hybridization chamber* for analyzing a component of said fluid sample (emphasis added).” Accordingly, Lipshutz here teaches at least two reaction chambers and a further hybridization chamber. This is not a capillary gap forms a single reaction chamber and is adapted to amplify and characterize nucleic acids therein as recited in claim 1.

Moreover, Lipshutz appears to require channels between its plurality of reaction chambers. Channels are defined as tubular passages for liquids, or courses or passages through which something may be moved or directed. The American Heritage Dictionary, Second College Edition, page 258. The present invention as defined by claim 1 has a single chamber that performs the required amplification and characterization in that single chamber without additional passages.

Lipshutz at col. 4, lines 22-25 states

one embodiment of the device of the invention will incorporate a *plurality of distinct reaction chambers* for carrying out the sample acquisition, preparation and analysis operations. In particular, a sample to be analyzed is introduced into the device whereupon it will be *delivered to one of several distinct reaction chambers*

which are designed for carrying out a variety of reactions as a *prelude* to analysis of the sample (emphasis added).

Here Lipshutz teaches that a plurality of reaction chambers carry out a variety of reactions. Lipshutz does not teach that any of its variety of chambers performs both reaction and analysis of a sample. In contrast, claim 1, recites “the capillary gap forms a single reaction chamber and is adapted to amplify and characterize nucleic acids therein.” Accordingly, Lipshutz does not teach a device having all elements of present claim 1 in as complete detail as is contained in claim 1.

Lipshutz at col. 17, lines 51-60 states

the device may incorporate a *plurality* of reaction chambers, storage chambers and analytical chambers, arranged in *series*, whereby a fluid sample is moved serially through the chambers, and the *respective operations* performed in these chambers. Alternatively, the device may incorporate a *central chamber* having the *various reaction/storage/analytical chambers* arranged around and fluidly connected to the central chamber, which central chamber acts as a sample gathering and redistribution hub for these various chambers (emphasis added).

Accordingly, Lipshutz does not here teach any capillary gap that forms a single reaction chamber that is adapted to amplify and characterize nucleic acids therein as recited in claim 1.

Lipshutz at col. 33, lines 29-31, claim recites a body having at least a *first reaction chamber* fluidly connected to a *second reaction chamber*.

Claim 1 recites, in part, “which the chamber body is sealingly placed to form a capillary gap between the chamber support and the detection area of the chip the capillary gap being temperature-adjustable and flow-controllable, and wherein the capillary gap forms a single reaction chamber that is adapted to amplify and characterize nucleic acids therein.” Applicant can not find these features in Lipshutz. For example, claim 1 recites the capillary gap forms a single reaction chamber that is adapted to amplify and characterize nucleic acids therein. Lipshutz does not teach such a feature. In fact, Lipshutz teaches a plurality of distinct reaction chambers, see e.g., col. 2, lines 16-20, Fig. 3, Figs. 5A, 5B, 6A and 6B along with the related text of Lipshutz. Still further, the Office Action admits that Lipshutz teaches that samples are put into one reaction chamber of the device and transferred to subsequent reaction chambers via fluid channels for controlled sample processing, fluid flow and nucleic acid amplification via

temperature adjustments. Moreover, applicant can not find where Lipshutz teaches or even suggests that a capillary gap is adapted to amplify and characterize nucleic acids as recited in claim 1.

Independent claim 1 also recites a “capillary gap”. Applicant can not find this feature in Lipshutz. A capillary cap is of extremely small dimensions. The term “capillary” is defined as of or relating to a tube with a fine bore. Oxford Dictionary of Biochemistry and Molecular Biology, 1997. Hence even minimal amounts of a sample can be used. Moreover, the extremely small dimensions of the capillary gap provide numerous control benefits that the common PCR chambers of Lipshutz does not provide. Applicant can not find capillary gaps as defined by claim 1 in Lipshutz.

Based at least on the foregoing, applicant submits that claim 1 and claims 2-19 and 25-43 depending therefrom are allowable over Lipshutz. Reconsideration and allowance are requested.

With regard to claim 2, the Office Action refers to column 19, lines 1-15 and column 24, line 34 – Column 25, line 41 of Lipshutz as teaching the subject matter of claim 2. Applicant can not find in this cited portion of Lipshutz any reference to a temperature adjustment means connected with the chamber support and adapted to permit a rapid temperature control the *capillary gap* as recited in claim 2. Reconsideration and allowance of claim 2 are requested.

With regard to claim 3, the Office Action refers to column 24, lines 34-63 and Fig. 2B, reference number 28, for a teaching of the subject matter of claim 3. Applicant traverses. Applicant can not find in this cited portion of Lipshutz the temperature adjustment means are situated on a side of the chamber support facing towards the chamber body as recited in claim 3. Reconsideration and allowance of claim 3 are requested.

Independent claim 25 recites, in part, “a capillary gap intermediate the chamber support and the chamber body, the capillary gap being adapted to act as a single chamber for both reaction and characterization of nucleic acids.” Applicant can not find these features in Lipshutz. In fact Lipshutz teaches that the amplification and characterization occur in distinct chambers.

The Office Action at page 8 states that

Lipshutz et al. disclose . . . a capillary gap intermediate the support and body, the gap adapted to act as a single chamber for both reaction (e.g. hybridization) and characterization (detection) of nucleic acids (e.g. Fig. 7A, Column 15, lines 9-34; and Column 19, lines 1-15 and column 24, line 34-Column 24, line 41).

Applicant traverses. As stated above Lipshutz merely teaches a plurality of reaction chambers each performing various functions. Applicant can not find in the cited portions of Lipshutz a teaching of capillary gap that is adapted to act as a single chamber for both the reaction and characterization of nucleic acids as recited in claim 25. Applicant requests a specific cite to where Lipshutz shows a capillary gap that acts as a single chamber for both reaction and characterization.

Applicant requests allowance of claim 25 and its dependent claims 26-30.

Independent claim 44 recites, in part, “a capillary gap intermediate the chamber support and the chamber body, the capillary gap consisting of a single chamber for both reaction and characterization of nucleic acids such that only the single chamber holds the nucleic acids for both reaction and characterization.” Applicant can not find these features in Lipshutz. Moreover, claim 44 uses the transitional phrase “consisting of”. This is a closed transistional phrase that limits the capillary gap to a single chamber as recited in the claim. See MPEP 2111.03. Accordingly, the capillary gap as recited in claim 44 can not have the plurality of chambers and channels of Lipshutz.

Allowance of claim 44 and dependent claim 45 is requested.

Claims 1, 2, 4, 5, 8-10, 12, 14, 15, 17-19, 25-30, 32, 34-36 and 39-45 were rejected under 35 USC § 102(e) as being anticipated by Woudenberg et al. (U.S. Patent No. 6,126,899). Applicant traverses as a *prima facie* case of anticipation has not been established.

Independent claim 1 recites, in part, “wherein the capillary gap forms a single reaction chamber that is adapted to amplify and characterize nucleic acids therein.” Applicant can not find these features in Woudenberg. Woudenberg relies on a plurality of interconnected detection chambers. See the drawing figures; column 26, lines 59-61; column 3, lines 27-28; and column 4, lines 23-25. Applicant can not find any reference in Woudenberg to a capillary gap as recited in claim 1. Accordingly, Woudenberg does not teach every element of the claim in as complete detail as is contained in the claim. Applicant requests withdrawal of the rejection and allowance of claim 1 and it dependent claims.

Claim 1 further recites, in part, “the detection area being adapted to immobilize at least one of nucleic acid molecules, peptides, and proteins.” Applicant can not find this feature in

Woudenberg. Applicant submits that the office action fails to indicate where Woudenberg shows a detection area as recited in claim 1. Moreover, applicant submits that Woudenberg teaches away from such a detection area as Woudenberg states at column 3, lines 8-18:

According to an important feature of the invention, the device is capable of maintaining a vacuum within the sample-distribution network (low internal gas pressure, relative to the external, ambient pressure outside the device) for a time sufficient to allow a sample to be drawn into the network and distributed to the detection chambers by vacuum action. For this purpose, the sample-distribution network may include a vacuum reservoir in fluid communication with, and downstream of, the detection chambers, for preventing the build-up of back-pressure in the network while the detection chambers are successively filled.

As a consequence such a device only allows the performance of homogenic assays, i.e., assays which are performed in one step since the vacuum prevents introduction of other reagents.

Hence, the assays of Woudenberg are performed by detection methods beginning at column 16, line 27 and the analytic specific reagents are not immobilized on a detection area. In contrast, the present device as defined by claim 1 requires a detection area being adapted to immobilize at least one of nucleic acid molecules, peptides, and proteins. Applicant requests withdrawal of the rejection and allowance of claim 1 and its dependent claims.

Dependent claim 4 recites, in part, the optically permeable zone of detection includes detection spots; and wherein the temperature adjustment means are configured such that the optical transparency of the chip remains unaffected at least at the detection spots. Applicant can not find these features in Woudenberg. The Office Action refers to Woudenberg's reference numbers 108 and 168 as showing detection spots. Applicant traverses. Woudenberg's reference numbers 108 and 168 are arrays of detection chambers (column 12, lines 21-22 and column 13, lines 57-58). Accordingly, the office action does not provide a *prima facie* case of anticipation with regard to claim 4. Withdrawal of the rejection of claim 4 is requested.

Dependent claim 15 recites the detection area is configured in the form of spots, onto which probes in the form of nucleic acid molecules are immobilized. Applicant can not find these features in Woudenberg. The Office Action refers to Woudenberg's reference numbers 108 and 168 as showing detection spots. Applicant traverses. Woudenberg's reference numbers 108 and 168 are arrays of detection chambers (column 12, lines 21-22 and column 13, lines 57-

58). Accordingly, the office action does not provide a *prima facie* case of anticipation with regard to claim 15. Withdrawal of the rejection of claim 15 is requested.

Independent claim 25 recites, in part, “a capillary gap intermediate the chamber support and the chamber body, the capillary gap being adapted to act as a single chamber for both reaction and characterization of nucleic acids.” Applicant can not find these features in Woudenberg. Woudenberg relies on a plurality of interconnected detection chambers. See for example, the drawing figures; column 26, lines 59-61; column 3, lines 27-28; and column 4, lines 23-25 of Woudenberg. Applicant can not find any reference in Woudenberg to a capillary gap as recited in claim 25. Accordingly, Woudenberg does not teach every element of the claim in as complete detail as is contained in the claim. Applicant requests withdrawal of the rejection and allowance of claim 25 and its dependent claims.

Independent claim 44 recites, in part, a capillary gap intermediate the chamber support and the chamber body and connected to the sample inlet and the sample outlet, the capillary gap consisting of a single chamber for both reaction and characterization of nucleic acids such that only the single chamber holds the nucleic acids for both reaction and characterization, and wherein the sample inlet and sample outlet are connected only to the single chamber. Applicant can not find all of these features in Woudenberg. For example, applicant can not find in Woudenberg the sample inlet and sample outlet are connected only to the single chamber as recited in claim 44. In contrast, Woudenberg shows a channel means 46a and 48a connecting inlet 38a to a plurality of detection chambers 44a in Fig. 2A. Woudenberg's Figures 2B, 2C, 3A-3C, 4, 5, 6A-6C, 7, and 8 all show the inlet connected to a channel means that connects to a plurality of detection chambers. In contrast to Woudenberg, claim 44 has the sample inlet only connected to the single chamber. Reconsideration and allowance of claim 44 and dependent claim 44 are requested.



§103 Rejection of the Claims

Claims 6 and 7 were rejected under 35 USC § 103(a) as being unpatentable over Lipshutz et al. (U.S. Patent No. 5,856,174) or Woudenberg et al. (U.S. Patent No. 6,126,899) in view of McBride et al. (U.S. Patent No. 6,296,752) as defined by Academic Press Dictionary of Science and Technology. Applicant respectfully traverses. While applicant believes that these claims include further distinguishing subject matter over the applied art, applicant does not comment at this time. Applicant merely asserts that claims 6 and 7 are allowable with their parent claim 1.

Claim 11 was rejected under 35 USC § 103(a) as being unpatentable Lipshutz et al. (U.S. Patent No. 5,856,174) or Woudenberg et al. (U.S. Patent No. 6,126,899) in view of Atwood et al. (U.S. Patent No. 5,475,610). Applicant respectfully traverses. While applicant believes that these claims include further distinguishing subject matter over the applied art, applicant does not comment at this time. Applicant merely asserts that claim 11 is allowable with their parent claim 1.

Claims 16, 17 and 37 were rejected under 35 USC § 103(a) as being unpatentable Lipshutz et al. (U.S. Patent No. 5,856,174) or Woudenberg et al. (U.S. Patent No. 6,126,899) in view of Fodor et al. (U.S. Patent No. 5,744,101). Applicant respectfully traverses. While applicant believes that these claims include further distinguishing subject matter over the applied art, applicant does not comment at this time. Applicant merely asserts that claims 16, 17 and 37 are allowable with their respective parent claims.

Telephone Interview Summary

The undersigned thanks the examiner for the courtesy of the telephone interview on 17 February 2005. The claims were discussed in view of the references applied to reject the claims. The differences between Lipshutz and the pending claims were discussed. No agreement as to allowance of any claims was reached.

Applicant requests a further telephone interview with the examiner if the application is not allowed in the next communication from the USPTO. The examiner can call the undersigned at 612-349-9587. The undersigned will call the examiner to set up a telephone interview. The

undersigned believes that such an interview will assist in moving this application to allowance or, at a minimum clarify issues for appeal.

Reservation of the Right to Swear Behind References

Applicant maintains its right to swear behind any documents which are cited in a rejection under 35 U.S.C. §§102(a), 102(e), 103/102(a), and 103/102(e). Statements distinguishing the claimed subject matter over the cited documents are not to be interpreted as admissions that the documents are prior art.

Conclusion

Applicant hereby incorporates all prior responses to preserve issues for appeal. Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 349-9587 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

RALF EHRLICH ET AL.

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Date

13 April '05

By

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 13<sup>th</sup> day of April, 2005.

CANDIS BUENDING

Name

Signature